10 51. (New Claim) The method of claim 50 wherein said compound is selected from the group consisting of

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cyclopentane heptenamide-5-cis-2-(3α-hydroxy-5-phenyl-1-trans-pentenyl)-3,5-dihydroxy, [1_α, 2_β, 3_α, 5_α];

cyclopentane N,N-dimethylheptenamide-5-cis-2-(3α–hydroxy-5-phenyl-1-trans-pentenyl)-3, 5-dihydroxy, [1_α, 2_β, 3_α, 5_α];

cyclopentane N-isopropyl hepteneamide-5-cis-2-(3α–hydroxy-5-phenyl-1-trans-pentenyl)-3, 5-dihydroxy, [1_α, 2_β, 3_α, 5_β];

cyclopentane N-ethyl heptenamide-5-cis-2-(3α–hydroxy-5-phenyl-1-trans-pentenyl)-3, 5-dihydroxy, [1_α, 2_β, 3_α, 5_α]; and

cyclopentane N-methyl heptenamide-5-cis-2-(3α–hydroxy-5-phenyl-1-trans-pentenyl)-3, 5-dihydroxy, [1_α, 2_β, 3_α, 5_α];

REMARKS

The present invention relates to certain novel cyclopentane heptanoic acid, 2-cycloalkyl or arylalkyl compounds, which may be substituted in the 1-position with hydroxy, amino, amido or ether groups, e.g., a 1- amido cyclopentane heptanoic acid, 2-(cycloalkyl or arylalkyl) compound and pharmaceutical compositions thereof. (See claims 21 and 22 and claims 23 and 24, as presently amended, respectively.) The cyclopentane heptanoic acid, 2-(cycloalkyl or arylalkyl) compounds of claims 21 and 22 of the present invention are potent ocular hypotensives, and are particularly suitable for the management of glaucoma. (See claims 1 through 10.) Moreover, the cyclopentane heptanoic, 2-(cycloalkyl or arylalkyl) compounds of this invention and related cyclopentane heptanoic acid, 2-(cycloalkyl or arylalkyl) compounds are smooth muscle relaxants with broad application in systemic hypertensive and pulmonary diseases; smooth muscle relaxants with application in gastrointestinal disease, reproduction, fertility, incontinence, shock, etc. (See claims 11 through 20, as amended.) Finally, claim 25 relates to

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the use of cloprostenol, fluprostenol and esters and salts thereof in the treatment of ocular hypertension and glaucoma.

The Examiner has rejected claims 7, 9, 17 and 19 under 35 USC § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which application regards as the invention. In particular, the Examiner argues that "(c)laims 7 and 17 recite the limitation " 'Y is O and X is selected from the group consisting of alkoxy and amido. There is insufficient antecedent basis for this limitation in the claim. Specifically, Y is never defined as O and X is never defined as amido. Further, claims 7 and 17 are dependent upon claim 5 which uses the variable Y^1 not Y". The applicants have amended claim 7 to replace Y with Y^1 and define Y^1 as Cl or trifluoromethyl. (See page 7, line 7, of the specification.) However, as to the Examiner's rejection of the term "amido", when X is $-N(R^4)_2$ and R^4 is a lower alkyl, X is an amido radical. The rejection of claims 7 and 17 is believed to be overcome by the present amendment of such claims, as is the Examiner's rejection of claims 9 and 19 for depending on an indefinite claim.

The Examiner has also advised the applicants "that should claims 2-10 be found allowable, claims 12-20 will be rejected under 35 USC § 101 as being a substantial duplicate thereof respectively. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to reject the other as being a substantial duplicate of the allowed claims."

The applicants have amended claims 12 through 20 and made them dependent on allowed claim 11 to overcome this rejection.

The Examiner has rejected claims 1 through 7 over various patents commonly owned by the Assignee of the present application. Applicants hereby offer a terminal disclaimer to remove this rejection as it pertains to U.S. Patents 5,607,978; 5,545,665; 5,352,708 and 5,587,391. It is believed that this Terminal Disclaimer overcomes this rejection.

The Examiner has rejected claims 1-4, 8, 10, 12, 13, 14, 18 and 20-25 under 35 USC § 102(e) as being anticipated by U.S. Patent 5,510,383 (hereinafter "Bishop"). The Examiner argues that "Bishop discloses the compound fluprostenol.... which is disclosed as being useful for the treatment of glaucoma and ocular hypertension. " The Examiner goes on to argue that "(w)hile applicants have a effective filing date of 9/21/92, the compound with CF_3 as the substituent on the phenyl was not disclosed therein. Applicants first disclosed this compound in the present application filed, 2/22/96. Further, the only support applicants have for the O-alkenylene linking moiety (the A portion of formula I) is in the present application and in examples 8, 9, and 15 of U.S. Patent 5,352,708 (application 07/948,056 parent application to the present application). Applicant is afforded the filing date of 2/22/96 for the above compound. Therefore, to prepare this compound and use it for the treatment of ocular hypertension is anticipated by Bishop as the reference discloses the compound fluprostenol in an ophthalmic composition for the treatment of glaucoma and ocular hypertension."

Claims 1-4, 8, 10, 12, 13, 14 and 20-24, as amended, are not anticipated by Bishop, in that only 1-amino, amido or ether derivatives are now claimed. None of these derivatives are disclosed or claimed by Bishop.

The applicants respectfully disagree with the Examiner's rejection of original claims 1-4, 8, 10, 12, 13, 14, 18 and 20-25 under 35 USC § 102 as being anticipated by Bishop, as well. First, it is clear that the applicants have disclosed that the alkenylene linking the omega chain to the cyclopentane ring may be substituted with the oxo group. This would include an oxo group at the terminal portion of the alkenyl radical wherein said radical links to B. This provides support for an O-alkenylene linking moiety as found in fluprostenol and cloprostenol. It is further clear that the applicants disclose in Example I, the compound 16m chlorophenoxy $PGF_{2\alpha}$ which is a specific example of a compound wherein the omega chain comprises oxygen-alkenylene linking group. This compound is also shown at Table V to be an effective IOP lowering agent both as an acid and as the 1-hydroxyl and 1-amido derivatives thereof. Note the methyl ester and the amido derivatives of 16-m-chloro phenoxy $PFG_{2\alpha}$ are prepared in Examples 8 and 9 of the present specification while the 1-hydroxy derivative is prepared in Example

15 of such specification. In addition to the above, the Bishop reference is not a statutory bar. That is, the publication date of Bishop is less than a year from the filing date of the present application. Thus applicant concurrently herewith submits a Declaration Under Rule 1.131 which demonstrates that prior to the filing date of Bishop the applicants had reduced to practice the present invention as related to fluprostenol in the United States.

Applicants have also amended claims 1, 21 and 22 to delete inadvertently claimed subject matter. In particular, claim 1, as originally filed, reads on the use of 16-[4-(methoxy)-phenyl]-17, 18, 19, 20 tetranor-$PGF_{2\alpha}$-isopropylester which is disclosed in EP 0364417A1, of record. This was unintentional and the above amendment deletes this unintentional inclusion. Claims 21 and 22 read on cloprostenol as a compound. This was also unintentional and is believed that by deleting cloprostenol specifically from claim 22 and amending claim 21 to require that when Z is =O, then X is not OR^4, applicants have placed claims 21 and 22, as presently amended, in condition for allowance.

Claim 25, as originally filed, substantially corresponds to claims 1 through 8 and 17 through 20 of Bishop. The applicants have added new claims 26 through 45 to specifically copy claims 1 through 20 of Bishop and request that the Examiner declare an interference to determine the priority of invention as to the subject matter of these added claims as well as claim 25. The claims copied from Bishop are in the present specification as follows:

Bishop, Claim 1 Woodward Claim 26	Support in Present Application
R^1 is hydrogen	Claim 1, X is OR^4 and R^4 may be hydrogen
R^1 is C_1-C_{12} alkyl, etc.	Claim 1, R^4 may be lower alkyl
R^1 is a pharmaceutically acceptable amine	Claim 1, compound of formula I, includes

	pharmaceutically-acceptable salts
R^1 is a cationic salt	Claim 1, compound of formula I, includes pharmaceutically-acceptable salts
R^2 is Cl or CF_3	Claim 4, Y^1 is Cl or trifluoromethyl
Bishop Claim 2 Woodward Claim 27 R^1 is H, CH_3, $CH(CH_3)_2$ and $C(CH_3)_3$	Claim 1 R^4 may be hydrogen or lower alkyl. See also, page 10, lines 25 and 26 wherein lower alkyl includes methyl, propyl and butyl
Bishop Claim 3 Woodward Claim 28 R^1 is Na^+ or $CH_3N^+(CH_2OH)_3$	Claim 1 includes pharmaceutically-acceptable salts. See also, page 13, line 5 wherein salt includes alkali metal salts
Bishop Claim 4 Woodward Claim 29 R^2 is Cl	See claim 4 wherein Y is Cl
Bishop Claim 5 Woodward Claim 30 R^2 is CF^3	See claim 4 wherein Y is trifluoromethyl
Bishop Claims 6-8 Woodward's Claims 31-33 between about 0.001 and about 1000 µg/eye of compound is administered	See page 13, lines 12-14 "therapeutically efficient amount is between about 0.0001 and 5% (w/v), preferably about 0.001 to about 1.0% w/v"

Bishop Claims 9-16 Woodward's Claims 34-41	Cover ophthalmic compositions useful in the method of claims 1-9 of Bishop and claims 26-33 of Woodward, respectively. The limitations of these claims mirror the limitations of the previously discussed method claims
Bishop Claim 17 Woodward Claim 42	
R^1 is a pharmaceutically acceptable ester moiety	See Claim 1, wherein Z is =O and X is $-OR^4$, wherein R^4 is a lower alkyl
R^2 is Cl or CF_3	See Claim 4 wherein Y^1 is Cl or trifluoromethyl
Bishop Claims 18-20 Woodward's Claims 43-45	(See discussion above.)

Applicants note that the Examiner has allowed claim 11. The applicants have amended claims 12 through 20 to depend on allowed claim 11 and it is presumed that these claims are also allowable.

It is noted that claims 5 through 7, 9, 11, 15 through 17 and 19 were only rejected for double patenting or under 35 USC § 112, second paragraph. It is believed that this amendment and the terminal disclaimer, filed herewith, overcomes these rejections. Applicants would appreciate it if the Examiner acknowledges that these claims are allowable.

Newly added claims 46 through 51 are more narrow in scope than original claims 5 through 7, 9, 11, 15 through 17 and 19 in that there is no alternative O-alkenylene linking group on the Y-chain and the phenyl group is unsubstituted. It would be appreciated if the Examiner also acknowledged the patentability of these claims.

Respectfully Submitted,

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